REMARKS

Claims 12-47 are pending in the application. Claims 12-21, 24-29 and the subject matter of the newly added claims 40 and 43-45 have been presently withdrawn from consideration as being directed to a non-elected invention. The subject matter of claims 22-23, and newly added claims 30-39, 41-42 and 46-47 have been examined on the merits. The amendments to claim 22 find bases at page 14 in the present specification. Support for the newly added independent claims 30 and 36 can be found in claims 2 and 5 as originally presented. Further, implicit support for "transfection effective carrier thereof" can be found in numerous places in the specification, including, *inter alia*, at page 20, paragraph 88; page 24, paragraph 108; and page 25, paragraphs 111-112. Newly added claims 31-35 find support in claims 3-6 as originally presented. Newly added claims 37-39 find support in claims 2-4 as originally presented. Newly added claim 40 finds bases in claim 12 as originally filed. Claim 41 finds bases in claim 22 as originally presented. Claim 42 finds bases in claim 23 as originally presented. Claim 43 finds bases in claim 24 as originally presented. Claims 44 finds bases in claim 25 as originally presented. Claim 45 finds bases in claim 27 as originally presented. No new matter has been inserted into the application.

Interview Summary

Applicant and Applicant's representative thank the Examiner for courtesies extended during the interview held on July 31, 2003. During the interview, the technology of the invention was discussed in detail, claim language was considered, and Hellmann (Virology. Vol. 143, pp. 295-303 (1985) was discussed. However, no agreement was reached.

Restriction Requirement

Applicants reserve the right to rejoin the subject matter of the non-elected method claims 12-21, 24-29 and newly added claims 40 and 43-45 to the currently examined claims, should the product claims currently under consideration be found to be allowable provided that the method claims are commensurate in scope with the allowable product claims.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1-11 have been rejected under 35 U.S.C. § 112, Second Paragraph, as being indefinite. Applicants traverse this rejection.

The Examiner objects to language such as "said antisense molecule" and "specifically binds" for either lacking antecedent bases or lacking clarity. Presently pending claims 12-47 do not recite these phrases. Thus, this rejection has been overcome.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 4-7 and 9 have been rejected under 35 U.S.C. § 112, First Paragraph, as allegedly failing to comply with the written description requirement. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

The Examiner states that claim terms "form", "derived from", and "substantially complementary" are not enabled by the specification. Presently pending claims 12-47 do not recite these phrases. Thus, this rejection has been overcome.

Rejection Under 35 U.S.C. § 102(b) Over Hellmann (Virology. Vol. 143, pp. 295-303 (1985))

Claims 1-3, and 5-11 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Hellmann. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

The Present Invention and Its Advantages

The present invention is directed to a composition comprising a large circular single-stranded nucleic acid molecule, which is at least about 3,000 nucleotides long and/or comprises a recombinant bacteriophage or phagemid genome, wherein the molecule comprises at least one target-specific antisense region, wherein the large circular single-stranded circular molecule is effective for reducing the expression of the gene; and a transfection effective carrier thereof.

Hellmann

Hellmann discloses an M13 molecule with a Tobacco Vein Mottling Virus insert sequence. Hellmann further discloses performing DNA:RNA hydridization assays with the M13 molecule in a reticulocyte lysate cell-free translation system, the so called hybrid-arrested translation system.

Hellmann fails to disclose or suggest mixing the M13 molecule with a transfection effective composition such as liposome, because Hellmann's assays with the M13 molecule is conducted entirely in a cell-free system, and there is no disclosure or suggestion found in Hellmann to combine the M13 molecule with any cell transfection reagent for introducing the M13 molecule into a cell.

Distinctions of the Claimed Invention Over the Cited Art

The Examiner is reminded that in order to reject a claim under §102, each and every element in the claim must be disclosed in the cited reference. In the present situation, Hellmann

fails to disclose or suggest including a reagent that is used for transfecting cells, as in the claimed invention. Therefore, Hellmann fails to anticipate the claimed inventive composition.

Rejection Under 35 U.S.C. § 102(b) Over Kool (WO 98/38300)

Claims 1-3, 22 and 23 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Kool. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

Kool disloses a circular oligonucleotide template, which is mixed with certain reagents and RNA polymerase to produce RNA products based on a rolling circle mechanism of RNA production. Kool discloses that "typically, a circular template has about 15-1500 nucleotides, preferably 24-500, and more preferably about 30-150." (Page 16, lines 13-15). Kool discloses that linear precircles may be ligated chemically or enzymatically to produce the circular form. (Page 18, lines 7-17). Further, Kool discloses at page 29, lines 18-20 that "because of their small size, the DNA circular vectors used as synthetic templates in the method of the invention are more easily introduced into cells than typical plasmid or viral vectors."

Kool fails to disclose or suggest the inventive composition directed to a large circular single-stranded nucleic acid molecule, which is at least about 3,000 nucleotides long and/or comprises a recombinant bacteriophage or phagemid genome, wherein the molecule further comprises at least one target-specific antisense region, wherein the large circular single-stranded circular molecule is effective for reducing the expression of the gene; and a transfection effective carrier thereof. In addition, Kool teaches away from the claimed invention because Kool specifically warns against using plasmid and viral vectors (see page 29, lines 18-20). For at least these reasons, Kool fails to anticipate the presently claimed invention.

Rejection Under 35 U.S.C. § 102(b) Over Moon (J. Biol. Chem. 275(18), pp. 4647-4653 (2000))

Claims 1, 3, and 11 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Moon. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

Moon discloses a ribbon-type antisense oligonucleotide. However, Moon fails to disclose or suggest the presently claimed inventive composition, which is directed to a large circular single-stranded nucleic acid molecule, which is at least about 3,000 nucleotides long and/orcomprises a recombinant bacteriophage or phagemid genome, wherein the molecule further comprises at least one target-specific antisense region, wherein the large circular single-stranded nucleic acid molecule is effective for reducing the expression of the gene; and a transfection effective carrier thereof. Therefore, Moon fails to anticipate the presently claimed invention.

Rejection Under 35 U.S.C. § 102(b) Over Yamakawa (Nucleosides & Nucleotides. Vol. 14, No. 3-5, pp. 1149-1152 (1995))

Claims 1, 3, and 11 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Yamakawa. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

Yamakawa discloses circularization of a 48-mer oligonucleotide. However, Yamakawa fails to disclose or suggest the presently claimed inventive composition, which includes a large circular single-stranded nucleic acid molecule, which is at least about 3,000 nucleotides long

and/or comprises a recombinant bacteriophage or phagemid genome, wherein the molecule comprises at least one target-specific antisense region, wherein the large circular single-stranded nucleic acid molecule is effective for reducing the expression of the gene; and a transfection effective carrier thereof. Therefore, Yamakawa fails to anticipate the presently claimed invention.

Rejection Under 35 U.S.C. § 102(b) Over LaPlante (Biochem J. Vol. 348, pp. 189-199 (2000))

Claims 1 and 4 have been rejected under 35 U.S.C. § 102(b) as being anticipated by LaPlante. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

LaPlante discloses an antisense cDNA for the gene encoding CHERP. However, LaPlante fails to disclose or suggest the presently claimed inventive composition, which includes a large circular single-stranded nucleic acid molecule, which is at least about 3,000 nucleotides long and/or comprises a recombinant bacteriophage or phagemid genome, wherein the molecule further comprises at least one target-specific antisense region, wherein the large circular single-stranded nucleic acid molecule is effective for reducing the expression of the gene; and a transfection effective carrier thereof. Therefore, LaPlante fails to anticipate the presently claimed invention.

Rejection Under 35 U.S.C. § 103(a) Over Hellmann in view of Hu '062 (U.S. Patent No. 6,107,062)

Claims 1-3, 5-11, 22 and 23 have been rejected as being obvious over Hellmann in view of Hu '062. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

Hellmann is discussed above.

Hu '062 discloses at col. 4, lines 5-15 a plasmid containing HIV-1 specific target sequences.

Distinctions of the present invention over the cited references

The Examiner has failed to establish *prima facie* obviousness of the present invention over the cited references. Hellmann discloses an M13 construct with a Tobacco Vein Mottling Virus insert sequence, which is used to create DNA:RNA hybrid as used in an *in vitro* cell-free hybrid arrest assay. Hu '062 is relied on for the disclosure of a plasmid that contains several target sequences. Applicants submit that the Hellmann reference and the Hu '062 patent fail to be combinable with each other. Whereas Hu '062 discloses a double stranded plasmid, the Hellmann reference is directed to a single-stranded M13 phage construct. Since the purposes for which each reference uses either the single-stranded or double-stranded form of either the phage or the plasmid vector are different, a person of ordinary skill in the art reviewing the Hellmann reference would not be motivated to consider using a plasmid DNA to solve the hybridization problem discussed in the Hellmann reference. And *vice versa*, a person reviewing Hu '062 column 4, lines 5-15 would not be motivated to consider the single-stranded M13 vector construct of Hellmann, as there is no simply no motivation found in either reference to combine these two references.

In further detail, Hellmann discloses using a single-stranded M13 based vector containing a target insert in which the obtained circular DNA binds to target RNA in a cell-free extract so that translation is arrested. In Hellmann, the single-stranded form of DNA itself is used as a probe to bind to a target RNA and arrest translation in a cell-free system. Therefore, a person considering the Hellmann reference and its experimental design would not look to a plasmid-

based double-stranded system as disclosed in Hu '062 at col. 4, lines 5-15, because such a plasmid based system would be useless in the experimental design of the Hellmann reference.

Hu '062 at col. 4, lines 5-15 discloses expressing antisense RNA sequence from a plasmid, wherein the RNA antisense sequence expressed from the plasmid DNA construct is used to bind and inhibit native target RNA. A person of ordinary skill in the art considering the Hu '062 reference would not be motivated to look toward using single-stranded M13 to express target specific RNA sequence, because the M13 construct in Hellmann is not used for expressing any target specific antisense RNA sequence from its M13 vector. Accordingly, Hu '062 and Hellmann fail to be combinable with each other.

In view of the above, the presently claimed invention cannot be said to be obvious over the cited Hellmann and Hu '062 references.

It is believed that the application is now in condition for allowance. Applicants request the Examiner to issue a notice of Allowance in due course. The Examiner is encouraged to contact the undersigned to further the prosecution of the present invention.

The Commissioner is authorized to charge JHK Law's Deposit Account No. **502486** for any fees required under 37 CFR §§ 1.16 and 1.17 that are not covered, in whole or in part, by a credit card payment enclosed herewith and to credit any overpayment to said Deposit Account No. **502486**.

Respectfully submitted,

JHK Law

Dated: August 29, 2003

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